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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/637,216	08/11/2000	Scott J Hultgren	WSHU2005.1	7884

321 7590 09/02/2003

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EXAMINER	
MARSCHEL, ARDIN H	
ART UNIT	**PAPER NUMBER**
1631	22

DATE MAILED: 09/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/637,216	HULTGREN ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-17,19-21 and 136* is/are pending in the application.

4a) Of the above claim(s) *20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-17 and 19* is/are rejected.

7)☒ Claim(s) *136* is/are objected to.

8)☒ Claim(s) *1,2,4-17,19-21 and 136* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *21* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' arguments, filed 1/30/02, have been fully considered and they are deemed to be persuasive to overcome previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Due to the newly applied rejections as set forth below, the finality of the Office Action, mailed 9/30/02, is hereby withdrawn. The Notice of Appeal, filed 1/30/02, is also therefore deemed moot.

SPECIE ELECTION REQUIREMENT

Due to the withdrawl of the rejections based on the elected SEQ ID NO: 12 which is deemed to be also within Formula I, the examination to hereby extended to include only the basic elections regarding Species A) and B) as set forth in the Office Action, mailed 5/8/01, Paper # 10. These remaining basic elections are A): peptide and B) *Escherichia coli*. Therefore, claims 1, 2, 4-17, 19, and 136 are under examination.

ABSTRACT

The abstract of the disclosure is objected to because it is too long and contains multiple paragraphs. A new abstract of 150 words or less is required. The new abstract is required to be submitted on its own separate sheet of paper. Correction is required. See MPEP § 608.01(b).

VAGUENESS AND INDEFINITENESS

Claims 1, 2, 4-17, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 3, the phrase "at least two alternating hydrophobic amino acid residues" is set forth. This phrase causes claim 1 to be vague and indefinite regarding what metes and bounds are meant thereby. The word "alternating" in said phrase is indicative of the practice of alternatives between which there is "alternating" practiced. Only hydrophobic amino acid residues are set forth in said phrase without defining at least one other alternative. What are at least two alternatives between which the alternating practice in said phrase is meant to define? A reasonable interpretation is that hydrophobic amino acid residues is one alternative. It may be conjectured that different hydrophobic amino acid residues are the alternatives as a possible interpretation. It is noted, however, that the limitation "different" is not set forth in said phrase in order to clearly define this practice. Another related unclarity in this phrase is what is meant by "two" alternating residues. The word "two" suggests that only two residues are required for the alternating practice. Thus, two different hydrophobic amino acid residues may satisfy this limitation. This is unclear, however, because alternating commonly is meant to define some type of back and forth changing practice with at least one change to one alternative and then a change back to the other starting alternative. This would require at least three residues and not only two as in said phrase. Yet another interpretation is that a pair, or at least two, hydrophobic residues are present where the pair alternatives back and forth in a sequence of amino acids in

the claimed compound. This alternating would require that the sequence be forward and then backward for the alternating practice of the pair, or at least two, hydrophobic amino acid residues. This is also not clearly stated as a sequence limitation in instant claim 1. In summary, the above several confusing and conflicting interpretations of said phrase supports this rejection in that instant claim 1 is vague and indefinite. It is noted that instant claim 4 specifically also contains this unclear phrase. Clarification via clearer claim wording is requested. Claims which depend directly or indirectly from claim 1 also contain this unclarity for embodiments which are described via the above unclear limitations due to their dependence.

In claim 1, there are two Z moieties defined as optionally being a peptide analog. These are the Z moieties labeled with subscripts 2 and 3. Consideration of the instant disclosure has failed to reveal a definition of the metes and bounds of what such an analog is. Without some definition of what is meant by such an analog, any change, addition, or deletion from some starting peptide could result in any resulting moiety of any length or composition. Thus, the metes and bounds of what is meant by such an analog are vague and indefinite. It is noted that instant claims 5, 9, 12, and16 also specifically contain this type of analogue limitation similarly without defined metes and bounds. Clarification via clearer claim wording is requested. Claims which depend directly or indirectly from claim 1 for embodiments which are described via the above unclear limitations also contain this unclarity due to their dependence.

In claim 7, the phrase "The mimic of claim 4" is set forth in line 1. This causes claim 7 to be vague and indefinite as to whether only the mimic is meant from claim 4 or

whether the subject matter of claim 7 is the "compound" of claim 4 but only with limiting mimic characteristics therein. Clarification as to antecedent basis in claim 7 is requested via clearer claim wording.

In claim 16, line 1, the phrase "antibacterial compound" is set forth without clear antecedent basis as to whether the compound of claim 1 is meant generically or a subset thereof. It is noted that claim 1 lacks a specific antibacterial compound citation. Clarification via clearer claim wording is requested.

Claims 13 and 17 are vague and indefinite as to whether the "further comprises" wording in line 1 of each claim is meant to direct the residue limitations therein to be further limitations of specific residues of the respective claims from which they depend or whether the residues are meant to be added segments beyond the sequences in claims 12 and 16, respectively.

LACK OF ENABLEMENT

Claims 6 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue

experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

Claims 6 and 10 are directed to modifications which result in improved binding, specificity, etc. This is also summarized in the specification on page 42, lines 5-11, but without any guidance general or specific for what results in such improvements. The instant specification describes various elements of 3-dimensional design of selection of peptides for inhibitory binding but lacks any description of what "improves" binding per se. It is well known that binding interactions which involve proteins are yet unpredictable even utilizing 3-dimensional modeling, such as from crystal structures. Applicants have neither specified what practices result in said improvements in the above listed claims, nor have overcome the unpredictability of protein or peptide binding parameters so as to enable said instant claims 6 and 10 regarding improvements which still are deemed unpredictable and thus support this rejection.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-12, 15, 16, and 19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Flemmer et al. [Bioorganic & Medicinal Chemistry Letters 5(9), pp. 927-932(1995)].

The title and Introduction section of the reference discloses the peptides therein as inhibiting complexation of bacterial chaperone papD as also required for instantly claimed peptides inclusive of antibacterial activity as required in instant claim 4. The first two paragraphs of the section therein entitled "Introduction" on pages 927 and 928 disclose the pili assembly chaperone domains as well as the presence of peptide segments in pap proteins which are pilus subunits in pili assembly. One of these peptides which is present in a pilus subunit protein is the G1'-G19' 19-mer peptide which is specifically set forth as to sequence on page 930 in the Figure 2 legend. This is described in the reference as a C-terminal segment of PapG. Instant claim 1 includes the limitation in lines 2-3 directed to a "mimic of an amino acid motif of a pilus subunit" which is interpreted to include the C-terminus peptide as described in the reference because a "mimic" is broadly defined in the instant specification on page 21, lines 11-14, as requiring only binding to a chaperone or another pilus subunit as an option therein. The Figure 2 legend in the first line describes the peptide as binding to the PapD chaperone thus meeting this mimic limitation although derived from the C-terminus rather than the amino terminus of a pilus subunit protein. It thus reasonably mimics chaperone binding. The G1'-G19' peptide is isolated and bound in a crystal

structure as disclosed in said Introduction section of the reference thus also anticipating the isolated limitation of the instant claims. The X and Z moieties of formula (I) of instant claims 1 and 12 are anticipated as follows:

$Z_1 - X_2$ is Gly(19') to Ser(11') noting that a peptide analog is inclusive of the 7-mer which is Gly(19') to Glu(13')

X_3 is Gly(10') which is hydrophobic

X_4 is Ser(9') which is any amino acid residue

X_5 is Met(8') which is a hydrophobic residue

X_6 is Thr(7') which is a hydrophobic residue

X_7 is Met(6') which is a hydrophobic residue

X_8 is Val(5') which is any amino acid residue

X_9 is Leu(4') which is an aliphatic residue

X_{10} is Ser(3') which is any amino acid residue

$Z_3 - Z_4$ is Phe(2')-Pro(1') which is either a peptide analog or a 2 residue peptide Thus, the limitations of instant claims 1 and 12 are specifically anticipated as well as instant claim 16 wherein the X_{13} to X_{17} residues correspond to X_3 to X_7 as noted above for the Gly(19')... peptide with the peptide analogs also in the instant claim 16 limitations being inclusive of the remainder of the reference's peptide or any amino acid residue as in X moieties 11 and 12 of said claim 16. It is lastly noted that increased binding efficacy characterized as increased inhibition for longer peptides such as the above described peptide is described in the reference on page 929, lines 14-17, which also anticipates the modification to improve binding in instant claims 6 and 10.

Claims 1, 2, 4-12, 15, 16, and 19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kuehn et al. [Science 262, pp. 1234-1241 (1993)].

Equivalent to the above peptide citations regarding the above rejection based on Flemmer et al. (1995) Kuehn et al. Also discloses the Gly(19') – Pro(1') peptide on page 1235 in Table 2. It is also noted that another peptide is therein disclosed with the same above residues which is cited as G1'-16' but with a shorter amino terminus which anticipates the instant Z_2 limitation in instant claim 1 via its being a 4 residue peptide given as KPGE thus not relying on the unclear peptide analog character but clearly being a 4 residue peptide as in said Z_2 residue.

OBJECTION

Claim 136 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

INFORMATION DISCLOSURE STATEMENTS

Enclosed is a re-executed PTO Form 1449, which was filed on 3/21/01. The re-execution is to correct an inadvertent oversight regarding citation numbered 28 thereon. The PCT search report has been reconsidered but cannot be properly listed on a PTO Form 1449 because it lacks a date of publication as required for all citations on a PTO Form 1449. It is noted that the Information Disclosure Statements, filed 11/20/00 and 3/21/01, have been reconsidered.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 29, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER